

55 YEAR OLD WOMAN WITH PNEUMONIA

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A 55 year old Caucasian female smoker, with past medical history significant for hypertension and peptic ulcer disease presented to the emergency department with a four day complaint of malaise, fever, and myalgias. She was seen by her primary care physician who started her on amoxicillin clavulanate for possible strep throat infection. Her family reported a productive cough with green sputum, pleuritic chest pain, nausea, vomiting and diarrhea for one week. They also felt she was getting more confused over the past several hours.

The patient was found to be confused, hypotensive, and hypoxic. Temp 98.1F, heart rate 107 beats per minute, respiratory rate 16 breaths per minute, blood pressure 73/51 mmHg, and oxygenating at 89% on room air. Physical exam revealed bilateral wheezing that was more prominent in the right lung field. She was tachycardic with no murmurs or rubs. The abdomen was soft and non-tender with no organomegaly and she had no evidence of a rash.

Labs on admission: WBC 2,600/mm³, Hemoglobin 13.3 g/dL, platelets 255,000/mm³, Na⁺ 134, K⁺ 4.5, HCO₃⁻ 19, BUN/Cr 49/2.8, AST 85, ALT 53. ABG: pH 7.2, PaCO₂ 49, PaO₂ 75, O₂ Sat 92%

The differential diagnoses at the time of presentation included community acquired pneumonia with *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catharalis* being high on the list of pathogens along with the atypical organisms such as *Legionella*, *Mycoplasma* and *Chlamydia*. Other infectious pathogens such as anaerobes and fungi are also included. Non-infectious etiologies including pulmonary embolism, vasculitis, hypersensitivity pneumonitis and neoplastic lymphangitis spread were also considered.

The patient was admitted to the ICU with presumptive admission diagnosis of septic shock secondary to pneumonia and was intubated within 1 hour of admission due to hypoxic respiratory failure requiring FIO₂ 100% and 16+ PEEP to maintain PO₂ of 70 mmHg. Stress dose steroids were started empirically, as well as empiric antibiotic coverage with azithromycin, piperacillin/tazobactam, and vancomycin. Recombinant human activated protein C was also administered 12 hours after admission. Two days later urine legionella antigen was found positive and antibiotics were switched to levofloxacin. The patient required pressure support for ten days and was extubated on the fifteenth day of hospitalization.

Epidemiology and clinical manifestations

First identified in 1976 during an outbreak at the annual meeting of the American Legion in Philadelphia (where out of 221 people infected, 34 died), *Legionella* is a facultative intracellular aerobic gram negative rod producing beta-lactamase, hardly visible on Gram stain due to its diminutive size. There are two major presentations of *Legionella* infection; the first being Legionnaires' Disease which is a community acquired pneumonia whose course can become very dramatic and the second being Pontiac fever



Figure 1. Chest X-ray revealing dense alveolar opacity at the right lung base with air bronchograms. There are left mid lung atelectatic changes and significant central vascular pulmonary congestion.

which is a more benign and self limited disease manifested through headaches, low grade fevers, malaise and chills without respiratory complaints and no radiological x-ray findings. Pneumonia is the most common clinical manifestation and *Legionella* has been reported as the third or fourth most commonly identified pathogen in community acquired pneumonias.^{1,2} However, it did account for only 4.7% of the CAP cases in one large study.³ Its prevalence is highlighted by the fact that it is also mentioned as one of the most common pathogens identified in nosocomial pneumonia.

Legionnaires' Disease

With an incubation period of two to ten days, this pathogen is considered transmitted through to the air conditioning and water cooling systems, rather than transmitted from person to person. Although first thought to manifest only as severe pneumonia (second only to *S. pneumoniae* in organisms identified in ICU admissions for pneumonia) accompanied by gastrointestinal symptoms and high fevers⁴⁻⁶, current diagnostic testing proved that presentation of *Legionella* infection may vary widely and that symptoms may be nonspecific.

Among the clinical clues for diagnosis of Legionnaires' disease are the gastrointestinal symptoms, especially diarrhea; neurological findings such as confusion, headache and lethargy; and fever > 39.0 C. Cough is usually mild and only slightly productive, hemoptysis is rarely encountered, and chest pain is infrequent. Physical exam is nonspecific with rales and subsequent signs of consolidation, fever as high as 40° C, bradycardia, lethargy, and stupor. Sputum gram stain shows WBC abundance but scant or no microorganisms. Hyponatremia (Na⁺ often less than 130)^{1,5-6,8}, hepatic and renal dysfunction, hematuria, thrombocytopenia and failure to respond to classic β lactam antibiotic treatment are often specifically seen in patients with *Legionella*. One should always maintain a higher index of suspicion for *Legionella* infection in patients considered at risk including smokers, those with chronic



Figure 2. CT of the chest showing dense right lower lobe consolidation, scattered areas of groundglass opacity and scattered focal nodular densities.

lung disease, and immunosuppressed patients such as those receiving steroids or anti-rejection drugs for post-organ transplant.

Radiological findings are usually already present by the third day of illness. Most commonly seen are patches consistent with unilobar infiltrates which may progress to consolidation. Pleural effusion may also be seen on x-ray, although infrequently⁹. In the immunosuppressed host, densities may appear as round opacities at the lung base, often progressing into cavitary lesions. Of note, radiological changes usually lag behind the clinical course, with complete resolution of the infiltrates within 4 weeks to several months from the debut of the illness.

Although some clinical manifestations are distinctive for *Legionella* infection, none of them are pathognomonic or highly specific. Early detection with prompt and appropriate antibiotic treatment have been proven to save lives^{10,11}. Culturing for *Legionella* spp. is the single most important laboratory test, but is time consuming and requires adequate respiratory specimen and a special culture media. Other tests have proved to be more beneficial: urinary antigen testing is rapid, sensitive, specific, and not costly. However, it is only useful for the diagnosis of *L. pneumophila* type 1 infection (accounting for 90 percent of community-acquired *Legionella* infections in the United States). The combination of culture of an appropriate respiratory specimen and urinary antigen testing are optimal as a diagnostic approach. Serologic tests, although available, are generally far less useful for the diagnosis of an individual patient but very useful for large epidemiological studies. While PCR-based tests exist, to date they do not exceed the sensitivity of culturing the organism. Given the severity and the high incidence of *Legionella* infection it is reasonable to perform specific diagnostic tests for all patients requiring hospitalization for community acquired pneumonia.

Treatment

The mortality of untreated or inadequately treated community acquired Legionnaires' disease is 16-30%, while the mortality for the nosocomial Legionnaire's disease may be as high as 50%¹². Timely use of the current diagnostic tests as well as prompt antibiotic treatment with active drugs have decreased mortality to less than 10%.

Although frequently used in the past, erythromycin has now been supplanted by newer macrolides as well as respiratory tract

quinolones. Two studies^{13,14} showed the higher efficacy of levofloxacin compared to macrolides as well as fewer complications and shorter hospitalizations. Current recommendations are a 7-10 day course of azithromycin or 10-14 day course of levofloxacin, with a longer 21 day course for immunosuppressed patients and patients requiring ICU admission. Given the high incidence and the severity of this disease, current recommendation for community acquired pneumonia requiring hospitalization is azithromycin either as monotherapy or along with β -lactame antibiotics^{15,16}. Monotherapy with an active quinolone is also acceptable. For nosocomial pneumonia, a quinolone (ciprofloxacin or levofloxacin) is the empiric drug of choice since the nosocomial infections are frequently associated with gram negative bacilli. For endocarditis and other extrapulmonary infections, a combination therapy is recommended with levofloxacin or azithromycin plus rifampin. Despite a significant decrease in mortality with prompt and proper antibiotic treatment, patients often have residual symptoms such as chronic fatigue syndrome (75%) and residual neurological deficits (63%).

Our case patient finished 21-day course treatment with levofloxacin for ARDS secondary to Legionnaires' disease. Hospital course was complicated by development of quadriplegia thought to be secondary to ICU neuropathy. Of note, *Legionella pneumophila* has also been linked independently with paraparetic complications. The patient did achieve further improvement in her neurological status and was able to be transferred to a rehabilitation facility. ■

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